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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/785,532	01/17/1997	JOE W. GRAY	2500.124US2	4124

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/785,532	GRAY ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-28,37 and 61-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-28,37 and 61-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/29/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on **03/30/05** has been entered.

Applicant cancels claim 56.

Accordingly, claims 26-28, 37, 61-63 are being examined.

The following are the remaining rejections.

INTERVIEW

The request for an interview in paper of 03/30/05 is acknowledged. However, a telephonic invitation for an interview with the Attorney Tom Hunter on 05/26/05 did not result in a response from Applicant.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claims 26-28, 37, 61-63 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of a method for detecting "colorectal" cancer claimed in Claims 26-28, 37, 61-63 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for "detection of amplification of the 20q13 amplicon is indicative of the presence of a large number of cancers, including colon cancer" (p.30, lines 9-11). There is however no mention of detecting "colorectal" cancer.

The subject matter claimed in claims broadens the scope of the invention as originally disclosed in the specification.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

Claims 26-28, 37, 61-63 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

The results from the determination of a gene copy number of a nucleic acid, i.e. whether it is an increase or a decrease or a change in the gene copy number of the tested sample as compared to the normal control, and

Correlating the results with the preamble.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Rejection under 35 USC 35 USC 112, first paragraph of claims 26-28, 61-63 pertaining to lack of a clear written description of a probe and the complement of SEQ ID NO:9, remains for reasons already of record in paper of 03/04/04.

Applicant recites the case law, stating that the written description does not require the Applicant to describe exactly the subject matter claimed, and that instead the description must clearly allow person of ordinary skill in the art to recognize what is claimed.

Suitable probe sequences are readily provided by routine use of probe design software packages or even by visual inspection of the sequence (for example the complement of SEQ ID NO:9) would readily be recognized as a suitable probe. Consequently, given the level of skill in the art, it is readily apparent that Applicants were in possession of the claimed invention.

Applicant's arguments set forth in paper of 03/30/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the probe in the claimed method is not limited to a sequence consisting of a fragment of SEQ ID NO:9, but encompasses an unrelated sequence, sharing with SEQ ID No:9 a common fragment, which is expected to specifically hybridizes under stringent conditions to its target sequences, including SEQ ID NO:9.

Contrary to Applicant's arguments, there is no disclosure of representative number of species of the claimed probes, nor a correlation between structure and function for the claimed probes, that would allow one to distinguish between that which is claimed from that which is not claimed.

The specification fails to describe the probe for use in the claimed method of detecting breast or colorectal cancer, by the standards set out in the example of Lilly. The specification describes only a single polynucleotide, SEQ ID NO: 9. Therefore, it

necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Further, it is noted a complement of SEQ ID NO:9 could be a partial or a complete full length complement, wherein a partial complement of SEQ ID NO:9 could share with SEQ ID No:9 only a few complementary nucleotides. In other words, the complement of the claimed method reads on unrelated sequence with unknown structure.

Thus, the specification does not meet the 112, first paragraph, written description of a probe, or a complement of SEQ ID NO:9, that is required to practice the claimed invention. Since the specification fails to adequately describe the product for use in the method of detecting breast or colorectal cancer, it also fails to adequately describe the method for detecting breast or colorectal cancer.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

A. Rejection under 35 USC 35 USC 112, first paragraph of claims 26-28, 37, 61-63, pertaining to lack of enablement for a method for detecting breast or colorectal cancer, remains for reasons already of record in paper of 03/04/04.

Applicant recites the reference by Collins et al, 1998, which teaches that ZABC1 (aka ZNF217) is centrally located in the 260 kb common region of amplification, and overexpressed in all cell lines and tumors in which it is amplified, and in two in which it is not.

Applicant recites the reference by Hidaki et al, 2000, which teaches that the level of 20q13.2 amplification correlates with the metastatic potential and tumor progression of colorectal cancer, and that the results suggest that 20q13.2 amplification with ZNF217 is associated with increased metastatic potential.

The recitation of Collins et al, and Hidaki et al is acknowledged and entered.

Applicant's arguments set forth in paper of 03/30/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that in the Exhibit A in the response of 09/16/03, shows the information from the web site http://www.infobiogen.fr/services/chromcancer/genes-gc/GC-ZNF127, which indicates that ZNF217 has as other name, ZABC1, at location 20q13.2.

However, no sequence comparison was provided, such that one could determine that the claimed ZABC1 comprising the genomic sequence of SEQ ID NO:9, having 10.365 kb in size, and the cDNA sequence of SEQ ID NO:10 of 3.186 kb, is the same as the ZNF217 taught in the art. Collins et al, 1998, teach that the genomic 15.7 kb ZNF127 comprises a cDNA sequence of 5632 bp, and two alternative spliced open reading frame of 3186 bp and 3324 bp (Collins et al, p.8707, second column, first paragraph). In view that no sequence comparison was provided, and further in view that the size of SEQ ID NO:9 is different from that of the ZNF127 gene taught in art, one cannot predict whether SEQ ID NO:9 is the same as the ZNF127 described in the art.

Further, even if SEQ ID NO:9 is the same as the ZNF217 taught in the art, one cannot extrapolate the teaching in the specification to the enablement of the claims,

because one cannot predict that SEQ ID NO:9 has an increased in copy number in breast or colorectal cancer.

It is noted that Collins et al, 1998, teach that the DNA fragments of ZNF127 are mapped to the distal end of the probe RMC20B4097, of 160 kb (, p.8706, second column, first 5 lines of second paragraph, and table 1 on page 8704), which is used for detecting amplification at 20q13.2 (p.8704, first column, paragraph under "Copy number analysis with interphase FISH). Collins et al teach that ZNF127 is centrally located in the 260-kb common region of amplification (abstract, p.8705, second column, last paragraph and figure 1, on page 8705).

Although ZNF127 is centrally located in the 260-kb common region of amplification of 20q13.2, however, one cannot predict that ZNF127, having only 15.7 kb in length, is amplified in breast cancer, because **the amplification of the 260-kb common region of 20q13.2 is not detected by the ZNF127 probe per se**, but by the probe RMC20B4097, of 160 kb, and because **the 260kb amplified region of 20q13.2 could contain several genes, and one cannot predict which genes or cluster of genes in said regions are amplified, in view that mutation is an unpredictable event.**

Further, Collins et al teach that ZNF127 is overexpressed in primary breast tumors in which it is amplified, but also in breast cancer cell lines in which it is not amplified (abstract, and p.8707, first column, first paragraph after figure 3 legend).

One cannot extrapolate from the overexpression of ZNF127 mRNA in breast tumor tissues as compared to normal breast tissue to amplification of ZFN127 gene in

breast cancer, because **one cannot predict that overexpression of ZNF127 mRNA is correlated with amplification of ZNF127 gene copy**, in view that ZNF125 mRNA is overexpressed in cells that have the amplication of the 260 kb region, as well as in cells that do not have the amplification of the 260 kb region (Collins et al, supra, abstract, and p.8707, first column, first paragraph after figure 3 legend).

Concerning amplification of SEQ ID NO:9 in colorectal cancer, even if SEQ ID NO:9 is the same as ZFN127, and although a locus of 20q13.2, that includes ZFN127 gene, is increased in copy number in colorectal cancer, as taught by Hidaka et al, 2000, however one cannot predict that SEQ ID NO:9 is amplified in colorectal cancer, because **the amplification is not detected by SEQ ID NO:9 per se**, but by a 20q13.2 **locus**-specific probe, wherein said probe comprises ZFN127 gene (Hidaka et al, 2000, page 2713, first column, paragraph under FISH), and because **the amplified locus of 20q13.2 could contain several genes, and one cannot predict which genes or cluster of genes in said regions are amplified, in view that mutation is an unpredictable event.**

In addition, the claims as written, encompass a method for detecting breast or colorectal cancer, comprising determining a copy number of "any nucleic acid" in the 20q13.2 region, and not necessarily the gene copy number of SEQ ID NO:9, nor is it necessary that said determined copy of the nucleic acid has an increase or decrease in its number.

One cannot extrapolate the teaching in the specification to the enablement of the claims, because in view that different genes have different structure, one cannot predict

that SEQ ID NO:9 could be used for determining the gene copy number of any other nucleic acids in the 20q13.2 region.

Further, in the absence of a disclosure in the claims concerning whether there is any change in the determined copy number of the nucleic acid as compared to the control sample, one would not know how to carry out the claimed method.

B. If Applicant could overcome the above 112, first paragraph, claims 26-28, 37, 61-63 are still rejected under 112, first paragraph for lack of enablement for a method for detecting breast or colorectal cancer, using "any probe of any structure" that selectively hybridizes under the stringent conditions cited in claim 26, for reasons already of record in paper of 03/04/04.

Applicant argues that the probe "specifically hybridizes or binds" the recited target sequence and not other non-related sequences that may be present.

Applicant recites a case law, stating that a patent needs not teach preferably omits what is well-known in the art. Applicant argues that given a known target sequence (SEQ ID NO:9), the design of suitable specific probes is routine.

Applicant's arguments set forth in paper of 03/30/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that "specifically hybridizes or binds" encompasses hybridizes or binds under high or very low specificity. Under very low specificity, the probes of the claimed method would bind to unrelated sequences.

Further, the probe in the claimed method is not limited to a sequence consisting of a fragment of SEQ ID NO:9, but encompasses an unrelated sequence, sharing with

SEQ ID No:9 a common fragment, which is expected to specifically hybridizes under stringent conditions to its target sequences, including SEQ ID NO:9, and unrelated sequences. Thus the case law is not applicable here, because the structure of the probe of the claimed method is not predictable.

C. If Applicant could overcome the above 112, first paragraph, claims 26-28, 37, 61-63 are still rejected under 112, first paragraph for lack of enablement for a method for detecting breast or colorectal cancer, using "any sample", e.g. any tissues other than breast or colorectal tissues, for reasons already of record in paper of 03/04/04.

Applicant argues that the claims clearly are directed to a method for detecting breast or colorectal cancer having an increased number of nucleic acid sequences at chromosome region 20q13.2 and not detecting any neoplastic cell.

Applicant's arguments set forth in paper of 03/30/05 have been considered but are not deemed to be persuasive for the following reasons:

The claims encompass a method for detecting breast or colorectal cancer, using "any sample", e.g. any tissues other than breast or colorectal tissues.

One cannot predict that tissues other than breast or colorectal tissues would have an increase in gene copy number of SEQ ID NO:9, because mutations of genes in different tissues are unexpected phenomena, and are independent of each other.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

June 01, 2005

SUSAN UNGAR, PH.D
PRIMARY EXAMINER